POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

Processing Requests for the Review of Grouped Supplements

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PURPOSE

- This MAPP outlines the policies and procedures for handling reviews of grouped supplements submitted to the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research (CDER). These procedures are intended to help OGD reviewers provide a consistent review of grouped supplements of five or more. Grouped supplements are multiple supplements submitted to abbreviated new drug applications (ANDAs) by a single applicant for the same chemistry, manufacturing, and controls (CMC) change to each application.[1]

BACKGROUND

- To improve efficiency in the application review process, OGD issued a letter on April 8, 1994, to all ANDA sponsors. That letter described procedures to be used by firms wanting to submit multiple supplements to cover an identical change to several different ANDAs. MAPP 5240.9 *Handling and Processing Requests for Global Reviews*, which published in 2004, replaced that letter.

[1] See the Guidance to Industry on *CMC Postapproval Manufacturing Changes Reportable in Annual Reports* (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM217043.pdf).

- This MAPP revises MAPP 5240.9 and changes the title to *Processing Requests for the Review of Grouped Supplements*.

POLICY

- OGD will:
  - Use the term "grouped supplements" instead of "global reviews" to refer to multiple ANDA supplements that propose the same CMC change from a single applicant.
  - Provide a consistent review of multiple ANDA supplements that propose the same CMC change from a single applicant.
  - Handle multiple supplements as grouped supplements if they meet the following criteria:
    - The supplements have the same date of submission on Form FDA 356h, *Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use* and are submitted to the OGD document room in a single package. If the supplement is submitted as a hardcopy, a duplicate copy of each supplement is included.
    - Each supplemental application clearly states on the cover letter the purpose of the proposed change and indicates that it is a part of a group of multiple submissions intended to be grouped together for review by OGD.
    - Each supplemental application is accompanied by an attachment listing the ANDA number and drug product for each supplemental application included in the total submission.
    - All supplements describe the identical change to each application, and there are no variances in individual submissions. (A group review is not appropriate if, for example, changes include individual stability data to support approval of each application.)
    - There are at least five individual supplements for the same change.
- When OGD determines that a grouped supplement is outside their purview (e.g., the grouped supplement contains an NDA or contains a microbiology supplement that doesn't require a chemistry review), designations are made.

RESPONSIBILITIES

- The grouped supplement coordinator (GSC):
    - Evaluates the appropriateness of the grouped supplements with the designated quality coordinator (DQC).
    - Designates the grouped supplement to a chemistry review team (CRT) if the grouped supplement submission meets the criteria.
    - Informs the applicant if the request to group the supplements together is denied.
- The DQC helps the GSC determine whether the supplements can be grouped together.

PROCEDURES

- The GSC receives an assignment from the document room on the lead ANDA of the grouped supplement and performs the following steps:
    - Reviews the cover letter of the supplement for appropriateness of the submission.
    - Checks that each submission has the same submission date.
    - Checks that each submission has a complete Form 356(h) that provides the correct sponsor information and ANDA number.
    - Checks that each supplement is accounted for in the document archiving, reporting and regulatory tracking system (DARRTS) under the designated group identification number.
    - Checks that the submission is properly categorized in DARRTS for the type of change and that the lead ANDA is designated properly.
    - Submits an establishment evaluation request (EER) for each of the supplements if the group requires facility evaluation for approval of the supplements.
    - Consults the DQC for final decision to grant or deny the supplements for a group review.
- The DQC reviews and determines whether each submission is for the identical change and appropriate supporting documentation is provided.

- The DQC makes the final decision to grant or deny the supplements for a group review and notifies the GSC.

- When the supplements are granted for a group review, the GSC performs the following steps:

    - Designates the grouped supplement to the CRT that has the most number of supplements in the group.

    - Notifies the designated product quality regulatory project manager (PM) and the CRT leader of the assignment. The GSC also files a memo in DARRTS with the designated CRT number and the list of the supplements in the group. The memo will include the rationale for the assignment.

    - If the grouped supplement includes any NDA supplements from ONDQA:

        - Contacts the ONDQA lead project manager (LPM) for the status of the grouped supplement in the Office of New Drug Quality Assessment (ONDQA) to take their lead in the review process.

        - Forwards ONDQA's review/correspondence to the designated PM for the grouped supplement when ONDQA finalizes the review of the NDAs.

    - If the granted grouped supplement contains sterile assurance information that warrants a review by the OGD Division of Microbiology:

        - Notifies the PM in the microbiology division and adds a microbiology assignment to the lead ANDA.

    - If the grouped supplement contains microbiology only supplements that do not require any chemistry review:

        - Forwards the supplements to the microbiology division PM. The PM coordinates with the microbiology division director or team leader to determine if the supplements can be reviewed as a group.

    - Designated CRT coordinates the review process of the grouped supplement and issues the supplement approval letter for the grouped supplement.

- When the supplements are denied for a group review, the GSC:

  - Notifies the OGD document room to separate the group of supplements and to assign each supplement to the appropriate review team.

  - Notifies the applicant that their supplements will not be reviewed as a group.

  - Enters the decision in DARRTS.

- When the PM receives the assignment for the grouped supplement he or she:

  - Designates the lead ANDA of the grouped supplement to one of the chemistry reviewers in the CRT and follows the general process for handling supplements submitted to OGD.

  - Asks the GSC from ONDQA for the review status if the supplements include an NDA.

- The chemistry reviewer and/or the CRT leader follow the general procedure for supplement review process; however, only the lead ANDA is designated for review. The remaining supplements in the group are referenced on the review/correspondence.

- If the grouped supplement qualifies for "By Inspection" review, the CRT leader conducts this review by following the general procedures for the review.

- If the grouped supplement is no longer deemed appropriate for a group review anytime during the review process, the chemistry reviewer and/or CRT leader notifies the PM to communicate this concern to the GSC.

- The designated PM informs the applicant that the grouped supplement will no longer be reviewed as a group with reasons provided by CRT.

- The designated PM notifies the GSC to initiate the separation of the grouped supplement.

- The GSC contacts the document room to separate the group and to assign each of the supplements to the responsible CRT.

- The GSC documents the group separation as a memo in DARRTS.

DEFINITIONS

- **Applicant:** A pharmaceutical firm or other party that submits a drug marketing application to FDA.

- **Grouped Supplements:** A group of supplements for five or more ANDAs that (1) cover an identical CMC change to each application; (2) are submitted by the same ANDA applicant; (3) can be reviewed by one reviewer; and (4) do not include unique data for each supplement.

- **OGD Group Supplement Coordinator:** The individual who organizes grouped supplement submissions, notifies appropriate personnel, and submits an EER to the Office of Compliance, if needed.

- **OGD Designated Quality Coordinator:** The individual who determines that each supplement submission in the group is for the identical change with appropriate supporting documentation to make the final determination to accept as grouped supplements.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
	1	Removed Attachment OGD document "Operating the Global SupplementSystem (GSS)."
	1	Revised procedures for review of grouped supplements.